

**REMARKS**

After the amendments above, claims 71, 74-77, 85-96 and 113-125 are pending. Claims 76-78, 80-84 and 89-112 previously were withdrawn from consideration by the Examiner.

Applicant thanks Examiner Steele for the courtesies extended during a telephone interview with the undersigned, Paul Wiegel, attorney for applicant, and Dr. Josef Prassler, Associate Director of R&D for applicant on July 7, 2009. The foregoing claim amendments and the discussion set forth below reflects the issues addressed during that interview, during which applicant proposed to present claims and analysis further clarifying the claimed invention and detailing the distinction between the claimed invention and the cited art.

*Support for the amendments*

The amendments to claims 71-77, and new claims 117-121 are fully supported by the specification, for example, at page 8, paragraphs 5 and 6; page 5, end of paragraph 3; page 3, paragraph 3; Figure 7a, Tables 3-4, first paragraph of page 7, the paragraph bridging pages 7 and 8, claim 10 as originally filed, and Example 2.1. The recitation that

said nucleic acid sequence encoding a variant of a wild type coat protein does not encode an interaction domain for interaction with a second domain present in said (poly)peptide/protein, and wherein the expression product of said nucleic acid sequence encoding said variant of a wild type coat protein and the expression product or products of any of said one or more nucleic acid sequences encoding a (poly)peptide/protein do not form a genetic fusion protein

is supported at page 2, second paragraph from bottom of page, page 5, fourth paragraph and page 3, second full paragraph.

The amendments to claims 75 and 77, and new claims 119 and 121 are supported by Tables 3-4, which show seven amino acids, for example DYCDIEF, which comprise a cysteine and page 10, second paragraph, which recites that one to six additional amino acids can be present.

***Restriction of Invention***

The Examiner requires a further election of an invention to be selected from Groups I-VI. Applicant provisionally elects with *traverse* Group IV, directed to a host cell comprising a nucleic acid sequence encoding a variant of a wild type bacteriophage coat protein comprising additions. Claims 71, 74-77, 85-96, 113-137 read on Group IV. The Examiner also acknowledges that claims 71-74 and 85-88 link the inventions I-VI and that claims containing all the limitations of an allowable linking claim will be rejoined upon indication of allowability.

***Priority***

The Examiner asserts that the priority documents, Application nos. EP99114072.4 and EP00103551.8 fail to provide adequate support or enablement in the manner required by 35 U.S.C. 112 for claim 75. Applicant respectfully traverses.

Instant claim 75 recites a modified variant comprising additional amino acid residues not present at the corresponding amino acid positions in a wild type coat protein of a bacteriophage, wherein one of said additional amino acid residues is a cysteine residue. EP99114072.4 with a priority date of July 20, 1999 states that the pIII expression cassette is under the control of the lac promoter/operator region comprising the signal sequence *ompA, amino acids DYCDIEF*, and the ORF for the mature gene III protein (emphasis added). See page 13 last paragraph, and page 14, first paragraph. In addition the entire sequences of the expression cassettes are provided on page 22 of the priority document. These sequences represent the sequences in Figures 6b and 6c in the present specification (10/658,752) as described at page 35 (of 10/658,752) each comprise the DYCDIEF motif, wherein the C represents a cysteine residue. Therefore, EP99114072.4 fully supports for claim 75.

EP00103551.8 with a priority date of February 18, 2000 states that the pIII or the pIIICT expression cassettes in the two vector system are under the control of the lac promoter/operator region and comprise the signal sequence *ompA, amino acids DYCDIEF*, and the pIII or pIIICT, wherein the complete amino acid sequences are provided in Table 3 (emphasis added). See page 19, second paragraph. Likewise, EP99114072.4 states in the one-vector system that the first expression cassette comprises the signal sequence *ompA, amino acids DYCDIEF*, and the ORF of the phage coat protein, wherein the amino acids sequences are provided in Table 4 (emphasis added). See page 19, last paragraph. Additionally, the full sequences of the C-gIII and C-gIIICT

are provided on page 31. Again these sequences represent the sequences in Figures 6b and 6c in the present specification (10/658,752) and as described at page 35 (of 10/658,752) each comprise the DYCDIEF motif, wherein the C represents a cysteine residue. Therefore, EP00103551.8 fully supports claim 75.

*Drawings*

The Examiner asserts that 37 CFR §§1.58(a) and 1.83(a) require that figures containing nucleic acid sequences be removed from the specification as duplicative of the sequence listing. Applicants respectfully point out that MPEP 608.02 states that

If a sequence listing as shown in the drawings has more information than is contained in the specification, the sequence listing could be included in the specification and the drawings.

The instant figures that contain sequences also contain information identifying the specific vectors that contain the sequences. This information is not contained in the sequence listing of the application. Accordingly, pursuant to MPEP 608.02, the sequences properly are included in the figures. Moreover, applicant further notes that deletion of the sequence-containing figures would require revisions throughout the specification and respectfully question the value of making such changes. Finally, this application is a divisional of an application that issued as Patent No. 6, 753, 136, where that patent contains the disputed sequence-containing figures. Requiring deletion of those figures from the instant application potentially would result in inconsistencies between the published specifications with no perceivable benefit. Applicant therefore respectfully requests that the objection be withdrawn.

*Rejection under 35 USC §112, first paragraph,*

The Examiner rejects claims 71-75, 79, and 85-88 under 35 U.S.C. § 112, first paragraph, for lack of written description. Support for the claims and any amendments thereto can be found as described above, and applicant respectfully requests that the rejection be withdrawn.

*Rejection under 35 USC §112, second paragraph*

The Examiner rejects claim 71, which recites the limitation “said nucleic acid encoding a coat protein” in line 10. Applicant has amended the claim to provide proper antecedent basis.

The Examiner has rejected claim 71, which recites the limitation “the poly/peptide protein” in line 6. Applicant has amended the claim to provide proper antecedent basis. The Examiner has rejected claim 71, which recites the limitation “said cysteine residue in said coat protein” in line the next to last line. Applicant has amended the claim to provide proper antecedent basis. The Examiner has rejected claim 71, which recites the limitation “said coat protein” in line 12 and 13. Applicant has amended the claim to provide proper antecedent basis. For the above reasons, applicant respectfully requests that this rejection be withdrawn.

***Rejection under 35 USC §102(b)***

The Examiner rejects claims 71-72, 74-75, 79 and 85-88 under §102(b) as being anticipated by Dower *et al.* U.S. Patent No. 5,427,908. The Examiner asserts that Dower teaches host cells comprising a vector comprising nucleic acids encoding a bacteriophage coat protein which has been fused to additional amino acids and comprising nucleic acids encoding a polypeptide comprising a cysteine residue. Applicant respectfully traverses. More specifically, Dower fails to describe each and every element of the claimed invention either in the claims as previously presented, or as presently amended, and therefore withdrawal of the rejection respectfully is requested.

Dower refers to two embodiments of phage fusions that display antibody fragments on the phage surface. In a first embodiment, one chain of a Fab fragment is genetically fused to a phage coat protein and the second chain of the Fab is expressed in a way that allows association of the two chains. In a second embodiment, a "tag protein ligand" is genetically fused to a phage coat protein and a "tag protein" is fused to a displayed protein, such as a heavy chain of a Fab pair, and the protein is displayed on the phage surface via association of the tag protein and the tag protein ligand. Neither embodiment of Dower meets each and every limitation of the instant claims and, accordingly, withdrawal of the rejection respectfully is requested.

The instant claims recite that the phage coat protein and the (poly)peptide/protein are not genetically fused, and this recitation specifically excludes Dower's first embodiment, where one chain of a Fab is genetically fused to a phage coat protein. Furthermore, although Fab fragments typically contain a disulfide bond between the CH1 and CL domains, it is well known that such fragments also associate via interaction domains. Thus, the heavy and light chains of a Fab fragment associate via interaction between VH and VL domains and via interaction of the CH1

and CL domains (see Padlan *et al.* and Pluckthun *et al.*, appended hereto as EXHIBITS A and B, respectively.) Indeed, the interaction between the CH1 and CL domains is sufficiently strong that many stable Fab fragments are known that contain no interchain disulfide bond between the Fab heavy and Fab light chains. (see Pluckthun, EXHIBIT B).

By contrast, the instant claims require that the encoded variant of a wild type coat protein variant does not contain an interaction domain, for example, a CH1 or CL domain, for interaction with a second domain present in the (poly)peptide/protein. This specifically excludes Dower's first embodiment where either the Fab heavy chain, which includes CH1 and VH interaction domains, or the Fab light chain, which includes CL and VL interaction domains, is fused to the phage coat protein.

Accordingly, Dower's first embodiment fails to teach each and every element of the claims and withdrawal of the rejection respectfully is requested.

With respect to Dower's second, "tag protein/tag protein ligand" embodiment, Dower makes no mention that the association between the tag protein and tag protein ligand can or should be via formation of a disulfide bond. To the contrary, the discussion at column 5, line 40 *et seq* of Dower clearly describes non-covalent types pf binding, rather than covalent disulfide bond formation. The nature of a tag protein/tag protein ligand interaction clearly requires the presence of an interaction domain fused to the phage coat protein, as in this embodiment the tag ligand is fused to the coat protein. Accordingly, Dower's "tag protein/tag protein ligand" embodiment does not teach each and every element of the instant claims and withdrawal of the rejection respectfully is requested.

#### ***Double Patenting***

The Examiner provisionally rejects claims 71-75, 79 and 85-88 on the ground of non-statutory obvious-type double patenting over claims 42-67 of co-pending Application No. 11/680,259. Applicant respectfully defers responding to this rejection as both applications are currently pending and subsequent amendments to the claims in either the present application or 11/680,259 likely will moot this rejection.

**CONCLUSION**

In view of the foregoing amendments, Applicants respectfully submit that the application is in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact the undersigned to expedite prosecution of the application.

The Commissioner is hereby authorized by this paper to charge any fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-3840. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. §1.136(a)(3).**

Respectfully submitted,



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Date: September 8, 2009

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